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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/484,340    06/07/95    SMITH    L    243132000105

ANTOINETTE F KONSKI  
MORRISON & FOERSTER  
755 PAGE MILL ROAD  
PALO ALTO CA 94304-1018

HM12/0527

EXAMINER

HOUTTEMAN, S

ART. UNIT

PAPER NUMBER

1634

DATE MAILED:

05/27/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
**08/484,340**

Applicant(s)  
**Smith et al.**

Examiner  
**Scott Houtteman**

Group Art Unit  
**1634**



☒ Responsive to communication(s) filed on Mar 3, 1999

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 75-77, 81-83, 88, 98, 100, 101, 103, 107, 109-132, and 136-146 is/are pending in the application.

Of the above, claim(s) 112-117 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 75-77, 81-83, 88, 98, 100, 101, 103, 107, 109-111, 118-132, 136-146 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to:

Art Unit: 1634; Examiner: Scott Houtteman.

2. Applicant's response, filed 3/3/99, has been carefully considered with the following effect:

The objection and rejections of paragraphs 5a, 5b, 5c, Office action mailed 8/26/98, have been withdrawn in view of applicant's amendments and arguments.

The objections and rejections of paragraphs 6, 7 and 8, Office action mailed 8/26/98, have been maintained.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 75-77, 81-83, 88, 98, 100-101, 103-105, 107, 109-11, 118-132 and 136-146 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Qu et al., Nuc. Acids Research, Sept. 1983, 11:5903-5920 (Qu); or Hindley, Proc. FEBS Symp: DNA-Recombination Interactions and Repair (1980) Pergamon Press, New York, pp. 143-154; (Hindley) in view of Langer et al., Proc. Natl. Acad. Sci, 78:6633-6637, Nov. 1981 (Langer) and Leary et al., Proc. Natl. Acad. Sci., 80:4045-4049, July 1983 (Leary) for reasons of record.

5. Applicant repeats the following arguments: that it is "impossible to produce a tagger primer . . . based on the teachings of Leary which allegedly might produce a heterogeneous collection of labeled probes. Applicant also argues that "a primer" refers to a population of nucleic acid molecules sharing a common sequence and capable of initiation of polymerization at a predetermined site.

Applicant also argues that the chromophore or fluorophore tagged oligonucleotides are "inherently detectable" while biotin-labeled oligonucleotides must be first bound with a labeled biotin ligand and that multiple labels can be used.

Applicant also argues that there is no motivation to combine the references because one is silent with respect to priming while others do not suggest tagging with biotin, chromophores or fluorophores.

Applicant argues that Best is distinguishable from the present case because applicant has pointed out differences between the claimed compositions and the prior art such as: covalent coupling of chromophore to fluorophores, inherently detectable and primer capability.

6. These arguments are not persuasive for the reasons of record. The following comments are intended to provide further emphasis.

The invention is not a method of use but a product claim. Thus, the claim reads on the product suggested in the prior art even if the use of the product suggested by the prior art is different from the use of the product disclosed in this application.

In this case, Applicant argues that primers are a population of molecules sharing a common sequence and capable of initiation of polymerization at a predetermined site. It is true that probes *can* be made up of a heterogeneous population. Nevertheless, probes are far more commonly a *homogeneous* population of molecules sharing a common sequence. This is so because the most common reagent used in a method of probe synthesis is a *homogeneous* population of cloned DNA.

Since the probe population is uniform, the probe population is also implicitly capable of initiation of polymerization at a predetermined site. This is because uniform initiation of polymerization is merely the result of priming from the 3' end of a uniform population of hybridized nucleic acids. The size of the hybridized nucleic acid is not relevant.

It is true that the average probe is larger than the average primer. Nevertheless, long primers can work as well as short ones. The main reason for the use of short primers is that the minimum size is about 20 or so bases. There is no theoretical maximum size.

7. Turning to applicants "inherently detectable" and "no motivation to combine" arguments, one finds these not persuasive. Simply put, the rejection sets fourth evidence that the chromophores and fluorophores labels were present in the prior art and are being used in the same way contemplated by the prior art, as labels for detecting the presence of nucleic acids.

It has not been disputed that the labels are found in the prior art. Further, it has not been disputed that there are no new methods for detection of these labels. The rejection merely assumes the labels would have been detected using prior art methods.

Thus, the rejection is based on the reasoning that labels used in one species of nucleic acid can be used in any species of nucleic acid and that one would be motivated, with reasonable expectation of success, to detect these labels using the appropriate prior art detection method. The motivation statement, to detect using prior art detection methods" has been directly addressed in the arguments.

8. Claims 75-77, 81-83, 88, 98, 100-101, 103-105, 107, 109-11, 118-146 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Qu or Hindley in view of Smith et al., US Pat. 5,118,800, 6/1992, eff. filing date 12/1983 (Smith) for reasons of record.

9. Applicant argues that there is no motivation to combine Smith with Qu or Hindley. This argument is not persuasive. The motivation has been set fourth by the examiner, for example, improving shelf-life, eliminating radioisotope use and permitting automation. See Office action mailed 8/26/98, page 9. These motivations have not been addressed in the arguments.

10. Claims 75-77, 81-83, 88, 98, 100-101, 103-105, 107, 109-11, 118-146 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Qu or Hindley in view of Levinson et al. (Biochim. Biophys. Acta, 447:260-273, 10/1976) (Levinson) for reasons of record.

11. Applicant argues that Levinson suggests only 1.44 acriflavine molecules per 100 bases and that "In certain embodiments of the invention, primers as short as 15 bases or shorter are used."

This argument is not persuasive.

) Firstly, it is the combination of references, not Levinson alone which is the basis of the rejection.

Furthermore, the legal conclusion of obviousness is made by "person of ordinary skill in the art." This person has attributed to him/her an up to date knowledge of all relevant scientific information (right up to the filing date of this application.) This person is hardly likely to dismiss all of the contemporary protocols addressing fluorophores and chromophore labels and, instead, use a standard from a *23 year old protocol* to judge the current state of enablement of fluorophore and chromophore labels.

When Levinson is viewed in context with the other publications and current scientific knowledge it is clear that there is a suggestion to combine the Levinson labels with the prior art primers for the reasons given in Levinson. Applicant has not addressed this motivation.

Finally, as stated previously, the claims are not limited to any particular method of use and so suggest the claimed products even if the intended use of the products suggested by the prior art differs from that use suggested in this application.

The claims must recite some physical limitation that is not met by the prior art. The claims are not limited to "primers as short as 15 bases or shorter."

12. Applicant's amendment made necessary the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

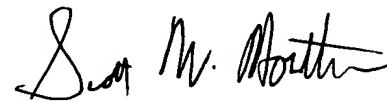
Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Technology Center 1600 Fax numbers are (703) 305-3014 and 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday from 8:30 AM - 3:30 PM. The examiner can also be reached on alternate Wednesdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

Scott Houtteman  
May 24, 1999



SCOTT W. HOUTTEMAN  
PRIMARY EXAMINER